ORIGINAL ARTICLE

Frontal lobe function in elderly patients with Alzheimer's disease and caregiver burden

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Abstract

Aim: Understanding of the relationship between caregiver burden and the degree of behavioural deficits in patients with Alzheimer's disease (AD) is relatively limited. Therefore, it is worthwhile to examine the correlations between the various relevant factors to improve the efficacy of care for patients with AD. The aim of this study was to investigate the specific contributions of frontal lobe dysfunction in AD patients to caregiver burden, while controlling for other predictor variables.

Methods: Participants included 30 pairs of caregivers and patients with AD. The Zarit Burden Interview and Frontal Assessment Battery were used to measure the caregiver burden and patients' frontal lobe function, respectively. To investigate the effects of frontal lobe dysfunction on caregiver burden, hierarchical regression equations with steps incorporating additional predictor variables were fitted. We also performed a correlation analysis between the individual subdomains of the Zarit Burden Interview and the predictor variables.

Results: Our study suggests that the degree of frontal lobe dysfunction in AD patients predicts their caregiver burden, when other factors of daily functional limitations and neuropsychiatric symptoms are controlled. Daily functional limitations and neuropsychiatric symptoms affected caregivers' psychosocial burden, whereas frontal lobe dysfunction affected caregivers' burden due to the increase in the dependency of the patients.

Conclusion: Our findings indicate that to ameliorate the disabilities of patients and reduce caregiver burden, there is a need for interventions that focus on psychosocial burdens, as shown in previous studies, as well as on excessive dependency due to frontal lobe dysfunction.

INTRODUCTION

The majority of patients with Alzheimer's disease (AD) and related disorders are cared for at home by family members.[1,2] Offering care for patients with dementia has a significant effect on the caregivers' emotional and physical health burdens. Caregivers have a higher risk of anxiety, depressive and sleep disorders, decreased quality of life, and an increased risk of cardiovascular morbidity and mortality.[2–8] Therefore, understanding the factors that contribute to caregiver burden is important for the realization of more effective psychosocial interventions aimed at improving the caregivers' quality of life.

Caregiver burden for the elderly consists of multiple dimensions, including time dependence and physical, emotional, developmental, and social burdens.[9] The functional decline of the patients is the main predictor of caregiver burden. The limitation of specific functions, such as the instrumental activities of daily living, increases the burden on caregivers of patients with dementia.[10] Across all cognitive domains, frontal system behavioural functioning has a larger influence on daily functioning than memory dysfunction.[11,12] Previous studies have indicated that frontal system behavioural problems of demented patients are predictive of caregiver burden after

controlling for dementia severity and caregiver depression.[13,14]

However, understanding of the association between caregiver burden and behavioural dysfunction in AD patients is still relatively limited, and it is necessary to examine the relationships in detail to improve the efficiency of care for patients with AD. This study investigated the contribution of frontal lobe dysfunction on caregiver burden. The Frontal Assessment Battery (FAB) was used to assess patients' frontal lobe function,[15] and the Zarit Burden Interview (ZBI) was used to measure caregiver burden.[16] Our aim was to acquire a better understanding of the details of frontal lobe dysfunction in AD patients in relation to the level of caregiver burden. Our overarching aim was to contribute to the development of interventions planned to relieve the distress of the caregiver.

METHODS
Subjects
Participants included 30 pairs of caregivers and AD patients with mild to moderate dementia. They were recruited from geriatric psychiatric outpatient clinics at a university hospital. All patients were diagnosed with probable AD based on the criteria of the National Institute on Aging and the Alzheimer's Association.[17] Patients were excluded if they had any neurodegenerative disease other than AD (e.g. dementia with Lewy bodies, Parkinson's disease, or Huntington's disease). Additionally, we excluded subjects with significant hearing or visual impairments that rendered interviews difficult. Each caregiver met the following inclusion criteria: (i) was a relative of the patient; (ii) was familiar with the patient's daily activities; and (iii) agreed to be interviewed. This study protocol was approved by the institutional review board of the university hospital and was performed in accordance with the Declaration of Helsinki (as revised in Brazil, 2013).

Measures
Caregiver burden was measured by the ZBI,[16] which is self-administered and consists of 22 items (scores range from 0 to 88). A higher score represents a higher burden.

Patients' frontal lobe functions were assessed with the FAB.[15] It is a brief bedside cognitive and behavioural battery for the assessment of frontal lobe function. It is relatively easy to administer and has good validity and reliability.[18] The FAB consists of six subtests that comprise conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. The total score is 18, and higher scores indicate better frontal functioning.

Patients' cognitive dysfunction was evaluated using the Mini-Mental State Examination (MMSE),[19] and the neuropsychiatric symptoms were assessed with the Neuropsychiatric Inventory (NPI).[20] Depression was assessed with the 15-item Geriatric Depression Scale.[21] Finally, functional capabilities were assessed using the Physical Self-Maintenance Scale (PSMS),[22] which consists of six items (using the toilet, feeding, dressing, grooming, physical ambulation, and bathing). Each item was scored on a scale from 0 (no impairment) to 4 (severe impairment), with a total range of 0–24 points.

Statistical analyses
Pearson correlation analyses were performed to investigate the relationships of each patient characteristic and each measurement (FAB, MMSE, NPI, PSMS, and Geriatric Depression Scale) with ZBI scores. Multivariate linear regression analyses were performed using a stepwise approach and included all the characteristics that were found to be significant in the correlation analysis. Estimates were adjusted for all the characteristics that remained significant at the final step. To investigate the relationship between frontal lobe dysfunction in the patient and perceived caregiver burden, hierarchical regression equations with steps incorporating predictor variables were fitted. Scores on the measures of the significant effects, other than FAB, were added in the first step to control for other predictor variables. FAB scores were added in the final step. Further, we conducted a second hierarchical regression analysis to investigate the specific domains of frontal dysfunction contributing to caregiver burden. Total scores on the ZBI served as the outcome variable in the regression analysis.

To investigate the relationship between the dimensions of caregiver burden and frontal lobe dysfunction and other significant predictor variables, we performed a partial correlation analysis between the individual subdomains of the ZBI and each predictor variable, after controlling for the other predictor variables.

Burden due to the three factors of psychosocial, dependency, and guilt was calculated as the mean of the three separate factors.[23] Psychosocial burden subscales included: 4, feels embarrassed; 5, feels angry; 6, relative affects relationships with others in negative way; 9, feels strained; 11, does not have privacy; 12, social life has suffered; 13, feels uncomfortable about having friends over; 16, unable to take care of relative much longer; 17, lost control of life; 18, wishes to leave the care to someone else; 19, feels uncertain; and 22, feels burdened. Dependency burden subscales included: 1, relative asks for more help than he/she needs; 2, not enough time for oneself due to time with relative; 3, stressed from trying to balance care and family/work responsibilities; 8, relative is dependent; 10, health has suffered because of involvement with relative; 14, are the only one that relative depends on; and 15, not enough money to take care of relative. Guilt burden included: 7, afraid of what the future holds for your relative; 20, should be doing more for your relative; and 21, could do a better job in caring for relative.

A P-value <0.05 was considered statistically significant. The multiplicity of the statistical analyses was considered to avoid type-I errors. SPSS (IBM Japan, Tokyo, Japan) version 22.0 was used for all descriptive and correlational analyses.

RESULTS

Patient characteristics and their associations with scores on the ZBI are presented in Table 1. Patients' gender, age, and educational level were not associated with the ZBI scores. The caregiver burden score was associated with frontal lobe dysfunction, as assessed by the FAB, as well as with the cognitive and behavioural problems reflected in the MMSE, NPI, and PSMS scores. When the significant variables associated with the ZBI were modelled together in a stepwise regression model, the NPI, PSMS, and FAB scores remained significant, whereas the MMSE score was not significant anymore.

To determine the relative effects of neuropsychiatric symptoms, physical activity in daily life, and frontal lobe dysfunction on caregiver burden, we used a hierarchical regression analysis with the total score on the ZBI as the dependent variable. We entered variables in the following order: (i) NPI; (ii) PSMS; and (iii) FAB scores. Results of the hierarchical regression analyses are presented in Table 2. NPI scores significantly accounted for the variance in the ZBI scores. PSMS scores added in the second step accounted for a significant increase in the variance of the ZBI scores. As predicted, FAB scores, added in the final step, accounted for a significant increase in the variance in the ZBI scores under the control of the NPI and PSMS scores.

We conducted a second hierarchical regression analysis to investigate the specific domains of frontal dysfunction contributing to caregiver burden (Table 3). The NPI scores and PSMS scores were entered, followed by the FAB subscale scores. Examination of individual predictors in these models indicated that the FAB subscale of conflicting instructions were significantly predictive of the ZBI scores.

In the correlation analysis between the three factors of the ZBI and the FAB, NPI, and PSMS

Table 1 Characteristics of patients and association with the Zarit Burden Interview

Variables	Mean ± SD or n (%)	Range	r[†]	P-value
Age (years)	73.0 ± 9.8	46–89	−0.22	0.24
Gender				
Male	8 (26.7%)	—	—	—
Female	22 (73.3%)	—	−0.06	0.75
Education (years)	11.8 ± 2.4	9–16	0.09	0.63
Measurements				
Zarit Burden Interview	12.6 ± 6.2	1–38	—	—
Frontal Assessment Battery	13.8 ± 3.7	4–18	−0.67	<0.001**
Mini-Mental State Examination	22.9 ± 3.2	13–26	−0.39	0.03*
Neuropsychiatric Inventory	2.7 ± 3.9	0–16	0.57	0.001**
Physical Self-Maintenance Scale	1.0 ± 1.8	0–7	0.55	0.002*
Geriatric Depression Scale	4.2 ± 4.0	0–13	0.13	0.51

*P < 0.05; **P < 0.001. [†] Results of Pearson correlation analyses performed to investigate the relationships between Zarit Burden Interview scores and each patient's characteristics and measurements.

Table 2 Hierarchical regression model relating burden to Neuropsychiatric Inventory, Physical Self-Maintenance Scale, and Frontal Assessment Battery

Hierarchical step	Predictor variables	Adjusted R^2	Change statistics		
			ΔR^2	ΔF	P-value (ΔF)
1	Neuropsychiatric Inventory	0.30	0.32	13.2	0.001**
2	Physical Self-Maintenance Scale	0.49	0.20	11.3	0.002*
3	Frontal Assessment Battery	0.55	0.08	5.12	0.032*

Total $R^2 = 0.60$, $F_{3,26} = 12.95$, $P < 0.001$. *$P < 0.05$; **$P < 0.001$.

Table 3 Hierarchical multiple regression analysis relating burden to Frontal Assessment Battery subscales

Step	Predictor variables	β	ΔR^2	P-value
1	Neuropsychiatric Inventory	0.36	0.32	0.01*
2	Physical Self-Maintenance Scale	0.30	0.20	0.04*
3†	Frontal Assessment Battery			
	Similarities	−0.04	0.19	0.79
	Verbal fluency	−0.10		0.48
	Motor sequence	0.23		0.13
	Conflicting instructions	−0.34		0.02*
	Go, no go	−0.21		0.18

*$P < 0.05$. †No patients showed the dysfunction in the prehension behaviour subscale of Frontal Assessment Battery.

measures (Table 4), the scores of the NPI and PSMS were mainly associated with psychosocial burden, whereas the FAB scores showed a correlation with the caregivers' burden due to the dependency of the patients. The FAB subscale of conflicting instructions was significantly predictive of both the psychosocial and dependency factors of the ZBI scores.

DISCUSSION

We found that frontal lobe dysfunction, daily functional limitations, and neuropsychiatric symptoms in AD patients were significantly correlated with higher caregiver burden. As predicted, the frontal lobe dysfunction of AD patients predicted their caregiver burden after we controlled for the other factors of daily functional limitations and neuropsychiatric symptoms.

The observed significant contribution of daily functional limitations and neuropsychiatric symptoms on caregiver burden is consistent with previous findings demonstrating that behavioural disturbance in the patient is one of the strongest contributors to caregiver burden.[13,24–28] Further, our study suggested that the degree of frontal lobe dysfunction in AD patients predicts their caregiver burden. Behavioural problems related to the frontal system have been shown to be

particularly burdensome.[13,14] Additionally, the level of distress associated with being a caregiver for a patient with behavioural variant frontotemporal dementia is higher than that of caregivers of patients with AD, possibly because frontal system behavioural problems are usually more prominent in frontotemporal dementia than in AD.[29–33] Our finding regarding the significant contribution of frontal lobe dysfunction replicated these previous results. Our findings also extend the previous findings: we demonstrated that this relationship between caregiver burden and frontal lobe dysfunction remains after we accounted for the variability of daily functional limitations and neuropsychiatric symptoms of the AD patients.

With regard to the FAB subscales, our findings indicated that ***'conflicting instructions (sensitivity to interference)' was predictive of burden, whereas other subscales were less burdensome to caregivers. The task of conflicting instructions challenges self-regulation in a behavioural interference paradigm; patients are instructed to execute one action in response to the observation of a different action, thereby requiring the inhibition of imitative response tendencies.[34–36] Patients with this dysfunction tend to display unintended imitative responses.[37] Although previous research suggested that objective measures of cognition are less reliably associated with burden,[14] the current study demonstrated that deficient self-regulation in a behavioural interference task is a strong predictor of caregiver burden.

Caregiver burden has various dimensions. The daily functional limitations and neuropsychiatric symptoms of patients significantly affected their caregivers' psychosocial burden. Previous studies of patients with dementia also demonstrated that patients' disabilities, including impairments in orientation, communication, financial, and transportation skills, are major predictors of the time-dependent burden.[10,38] The current results implied that the patients' functional disabilities and

Table 4 Partial correlations between three factors of the Zarit Burden Interview and predictor variables[†]

Variables	Psychosocial	P-value	Dependency	P-value	Guilt	P-value
NPI	0.65	<0.001*	0.12	0.54	0.16	0.42
PSMS	0.63	<0.001*	0.12	0.55	0.39	0.04
FAB	−0.37	0.06	−0.48	0.01*	−0.07	0.73
Similarities	−0.18	0.35	−0.30	0.12	0.009	0.96
Verbal fluency	−0.18	0.37	−0.27	0.16	−0.19	0.34
Motor sequence	−0.13	0.50	0.02	0.93	0.27	0.16
Conflicting instructions	−0.50	0.007*	−0.53	0.004*	0.28	0.15
Go, no go	−0.13	0.50	−0.42	0.03	0.18	0.35

*$P < 0.0166$ (0.05/3). [†] Other predictor variables are covariates.
FAB, Frontal Assessment Battery; NPI, Neuropsychiatric Inventory; PSMS, Physical Self-Maintenance Scale.

neuropsychiatric symptoms directly relate to psychosocial burden, including time pressures and the caregivers' feelings of being psychosocially isolated. The caregiver is required to take over the patient's everyday tasks and manage the neuropsychiatric symptoms, thereby creating the greatest time demand and level of psychosocial isolation. Our results indicated that interventions to address problems of psychosocial burdens have the potential to be particularly helpful in reducing the carer burden of caregivers of patients with daily functional limitations and neuropsychiatric symptoms.

Frontal lobe dysfunction was also shown to affect caregiver burden, in addition to the psychosocial burden, due to patients' increased dependency. A caregiver's feelings about a patient's excessive dependency may be induced by the patient's poor self-regulation in the behavioural interference paradigm. These findings indicated the clinical importance of implementing interventions for reducing caregiver burden that focus on both psychosocial burden and a patient's excessive dependency due to frontal lobe dysfunction. In clinical settings, interventions designed to improve caregiver understanding of the specific changes in the patient's dependency may be beneficial. Specifically, well-designed psychoeducational interventions could help to reduce caregiver burden by helping caregivers understand the changes inherent to frontal lobe dysfunction.[39] This would allow caregivers to adjust their expectations, leading to acceptance of the diagnosis and helping them overcome the difficulties of the situation.[29]

This study had some limitations. First, in contrast to epidemiologic data that rest on large population studies, our data of 30 individuals recruited from the geriatric psychiatric outpatients clinic at a university hospital are not based on random sampling selection. Second, this was a cross-sectional survey and not a longitudinal follow-up study; this format limited our ability to make causal inferences from this study. Finally, a more sophisticated frontal function measure, in addition to the FAB, is recommended in future studies. Neuroimaging technology is one such alternative method for defining frontal lobe function.[12] The findings of our pilot study need confirmation with further studies using a prospective design, larger sample size, and a more precise measure of frontal function to address these issues.

In conclusion, our study suggested that frontal lobe dysfunction in AD patients predicts caregiver burden, after other factors of daily functional limitations and neuropsychiatric symptoms are controlled. Daily functional limitations and neuropsychiatric symptoms affected caregiver psychosocial burden, whereas frontal lobe dysfunction affected caregiver burden due to increased patient dependency. Given these correlations, further studies should examine interventions focused on excessive patient dependency due to frontal lobe dysfunction in order to ameliorate the specific disabilities of patients and reduce caregiver burden.

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REFERENCES

1 Aneshensel CS, Pearlin LI, Schuler RH. Stress, role captivity, and the cessation of caregiving. *J Health Soc Behav* 1993; **34**: 54–70.
2 Stommel M, Collins CE, Given BA. The costs of family contributions to the care of persons with dementia. *Gerontologist* 1994; **34**: 199–205.

3 Garand L, Dew MA, Eazor LR, DeKosky ST, Reynolds CF III. Caregiving burden and psychiatric morbidity in spouses of persons with mild cognitive impairment. *Int J Geriatr Psychiatry* 2005; **20**: 512–522.

4 Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: a prospective study. *Am J Prev Med* 2003; **24**: 113–119.

5 Schulz R, Beach SR. Caregiving as a risk factor for mortality: the caregiver health effects study. *JAMA* 1999; **282**: 2215–2219.

6 Seeher K, Low LF, Reppermund S, Brodaty H. Predictors and outcomes for caregivers of people with mild cognitive impairment: a systematic literature review. *Alzheimers Dement* 2013; **9**: 346–355.

7 von Kanel R, Mausbach BT, Patterson TL *et al.* Increased Framingham coronary heart disease risk score in dementia caregivers relative to non-caregiving controls. *Gerontology* 2008; **54**: 131–137.

8 Wolf-Maier K, Cooper RS, Banegas JR *et al.* Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA* 2003; **289**: 2363–2369.

9 Caserta MS, Lund DA, Wright SD. Exploring the Caregiver Burden Inventory (CBI): further evidence for a multidimensional view of burden. *Int J Aging Hum Dev* 1996; **43**: 21–34.

10 Razani J, Kakos B, Orieta-Barbalace C *et al.* Predicting caregiver burden from daily functional abilities of patients with mild dementia. *J Am Geriatr Soc* 2007; **55**: 1415–1420.

11 Kiosses DN, Alexopoulos GS, Murphy C. Symptoms of striatofrontal dysfunction contribute to disability in geriatric depression. *Int J Geriatr Psychiatry* 2000; **15**: 992–999.

12 Chen HM, Hou SY, Yeh YC *et al.* Frontal function, disability and caregiver burden in elderly patients with major depressive disorder. *Kaohsiung J Med Sci* 2010; **26**: 548–554.

13 Rymer S, Salloway S, Norton L, Malloy P, Correia S, Monast D. Impaired awareness, behavior disturbance, and caregiver burden in Alzheimer disease. *Alzheimer Dis Assoc Disord* 2002; **16**: 248–253.

14 Davis JD, Tremont G. Impact of frontal systems behavioral functioning in dementia on caregiver burden. *J Neuropsychiatry Clin Neurosci* 2007; **19**: 43–49.

15 Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a frontal assessment battery at bedside. *Neurology* 2000; **55**: 1621–1626.

16 Zarit SH, VandenBos GR. Effective evaluation of memory in older persons. *Hosp Community Psychiatry* 1990; **41**: 9–10, 16.

17 Sperling RA, Aisen PS, Beckett LA *et al.* Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 2011; **7**: 280–292.

18 Moorhouse P, Gorman M, Rockwood K. Comparison of EXIT-25 and the Frontal Assessment Battery for evaluation of executive dysfunction in patients attending a memory clinic. *Dement Geriatr Cogn Disord* 2009; **27**: 424–428.

19 Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**: 189–198.

20 Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994; **44**: 2308–2314.

21 Lesher EL, Berryhill JS. Validation of the geriatric depression scale--short form among inpatients. *J Clin Psychol* 1994; **50**: 256–260.

22 Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; **9**: 179–186.

23 Stinson JM, Collins RL, Maestas KL, Pacheco V, LeMaire A, Benge J. Dependency aspect of caregiver burden is uniquely related to cognitive impairment in veterans. *J Rehabil Res Dev* 2014; **51**: 1177–1188.

24 Baumgarten M, Battista RN, Infante-Rivard C, Hanley JA, Becker R, Gauthier S. The psychological and physical health of family members caring for an elderly person with dementia. *J Clin Epidemiol* 1992; **45**: 61–70.

25 Pinquart M, Sorensen S. Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 2003; **58**: P112–P128.

26 Clyburn LD, Stones MJ, Hadjistavropoulos T, Tuokko H. Predicting caregiver burden and depression in Alzheimer's disease. *J Gerontol B Psychol Sci Soc Sci* 2000; **55**: S2–S13.

27 Donaldson C, Tarrier N, Burns A. The impact of the symptoms of dementia on caregivers. *Br J Psychiatry* 1997; **170**: 62–68.

28 Nagaratnam N, Lewis-Jones M, Scott D, Palazzi L. Behavioral and psychiatric manifestations in dementia patients in a community: caregiver burden and outcome. *Alzheimer Dis Assoc Disord* 1998; **12**: 330–334.

29 Mioshi E, Foxe D, Leslie F *et al.* The impact of dementia severity on caregiver burden in frontotemporal dementia and Alzheimer disease. *Alzheimer Dis Assoc Disord* 2013; **27**: 68–73.

30 Mioshi E, Bristow M, Cook R, Hodges JR. Factors underlying caregiver stress in frontotemporal dementia and Alzheimer's disease. *Dement Geriatr Cogn Disord* 2009; **27**: 76–81.

31 de Vugt ME, Riedijk SR, Aalten P, Tibben A, van Swieten JC, Verhey FR. Impact of behavioural problems on spousal caregivers: a comparison between Alzheimer's disease and frontotemporal dementia. *Dement Geriatr Cogn Disord* 2006; **22**: 35–41.

32 Boutoleau-Bretonniere C, Vercelletto M, Volteau C, Renou P, Lamy E. Zarit Burden Inventory and activities of daily living in the behavioral variant of frontotemporal dementia. *Dement Geriatr Cogn Disord* 2008; **25**: 272–277.

33 Riedijk SR, De Vugt ME, Duivenvoorden HJ *et al.* Caregiver burden, health-related quality of life and coping in dementia caregivers: a comparison of frontotemporal dementia and Alzheimer's disease. *Dement Geriatr Cogn Disord* 2006; **22**: 405–412.

34 Lhermitte F, Pillon B, Serdaru M. Human autonomy and the frontal lobes. Part I: imitation and utilization behavior: a neuropsychological study of 75 patients. *Ann Neurol* 1986; **19**: 326–334.

35 De Renzi E, Cavalleri F, Facchini S. Imitation and utilisation behaviour. *J Neurol Neurosurg Psychiatry* 1996; **61**: 396–400.

36 Brass M, Derrfuss J, Matthes-von Cramon G, von Cramon DY. Imitative response tendencies in patients with frontal brain lesions. *Neuropsychology* 2003; **17**: 265–271.

37 Kopp B, Rosser N, Tabeling S *et al.* Performance on the frontal assessment battery is sensitive to frontal lobe damage in stroke patients. *BMC Neurol* 2013; **13**: 179.

38 Marvardi M, Mattioli P, Spazzafumo L *et al.* The caregiver burden inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study. *Aging Clin Exp Res* 2005; **17**: 46–53.

39 Chan SW. Family caregiving in dementia: the Asian perspective of a global problem. *Dement Geriatr Cogn Disord* 2010; **30**: 469–478.